REMARKS

SECOND PRELIMINARY AMENDMENT

With this response Applicants submit new claims 41 to 71 which possess unity of invention with at least the claims of Groups VI and XII specified in the restriction requirement dated February 11, 2003. Support for these new claims is found in the specification on page 11, lines 16-21 and on page 19, lines 1-13 and lines 20-26. Claims 41 and 56, which specify sequencing methods, and claims 48 and 63, which specify hybridization methods for detection of mutations or polymorphisms, find support at page 19, line 30 to page 20, line 17 of the application. Claims 46, 53, 61, 68, which relate to amplification steps, find support at page 8, lines 27-35 and page 9, lines 8-27.

Claims 42, 49, 57, 64 which relate to the use of genomic DNA, find support at page 19, lines 8-9. Claims 43, 50, 58, 65, which relate to the use of cDNA, find support at page 9, lines 28-34. Claims 44, 51, 59, 66, relating to the use of a biological sample for antenatal diagnosis, find support at page 19, lines 21-26. Claims 45, 52, 60, 67, which relate to the use of lymphoblasts, find support at page 22, lines 30-31. Claims 47, 54, 62, 69, 71, which relate to the use of primers comprising SEQ ID Nos. 4-71, find support at page 8, lines 4-5, and in Table 2.

Applicants respectfully ask that new claims 41 to 71 be entered at this time. Applicants also wish to call the Examiner's attention to claims 10, 11, 24 and 25, which are presently amended to conform more closely to U.S. practice. Applicants respectfully ask that these amendments be entered as well.

RESPONSE TO RESTRICTION REQUIREMENT

In response to the Restriction Requirement dated February 11, 2003, Applicants elect the claims of Group XII with traverse. The claims of Group XII (presently claims 31 and 32) are drawn to a method for diagnosis of an autosomal dominant form of hereditary spastic paraplegia (AD-HSP). This response also includes a second preliminary amendment, adding claims 40-71, which are also drawn to methods for diagnosis of hereditary spastic paraplegia. Applicants reserve the right to prosecute non-elected claims in continuing applications or take other such actions as deemed necessary to protect the non-elected inventions. Applicants do not waive any rights in the non-elected inventions.

Further, Applicants elect SEQ ID No. 1 as the elected species with traverse. Claims 1, 2, 5, 8-22 and 24-32 are believed to read on the elected species.

The present application was filed under 35 U.S.C. § 371(c), as a U.S. National Stage application. Accordingly, under 37 C.F.R. § 1.475(a), the national stage application must relate to only one invention or to a group of inventions that are linked as to form a single general inventive concept to meet the requirement of unity of invention. Where a group of inventions is claimed in an application, the requirement of unity of invention can be fulfilled when there is a technical relationship among those inventions, which involves one or more of the same or corresponding special technical features. Special technical features are those technical features that define the contribution of the claimed subject matter over the prior art when each of the claimed inventions is considered as a whole. Moreover, under 37 C.F.R. § 1.475(b)(2) a national stage application containing claims to

different categories of invention will be considered to have unity of invention if the claims are drawn to a product and a process of use.

The general inventive concept of the present invention is a method to diagnose autosomal dominant hereditary spastic paraplegia. The method uses nucleic acid molecules comprising portions of the nucleotide sequence of the human SPG4 gene.

Contrary to the Examiner's assertion, the SPG4 gene is not identified in the Kikuno et al. publication. Neither the Kikuno publication nor the sequence at GeneBank Accession No. AB029006 identifies the mRNA sequence of Kikuno as the nucleotide sequence of the human SPG4 gene, nor does it suggest that in some individuals, mutations of the SPG4 gene cause the disease autosomal dominant hereditary spastic paraplegia.

The claims of the present application are generally drawn to methods of detecting nucleotide sequence differences in the SPG4 gene that may indicate a diagnosis of AD-HSP, or to the diagnostic tools that can be used in making such a diagnosis (*e.g.*, nucleic acids, vectors and host cells comprising those nucleic acids, polypeptides, antibodies) or methods to produce those tools. Thus, the claims are drawn to a product, the nucleotide sequences and to a process of use of the product, the method of diagnosis.

The Examiner asserts that a nucleotide sequence is a "special technical feature," and focuses narrowly on a single "group" of claims to find that technical feature. A technical feature does not have to be based narrowly on a single chemical or chemical structure. In dividing the groups of claims, the Examiner uses concepts and terminology found in restriction practice of the U.S. Patent Office that are not used under the principles of unity of invention. The Examiner's criteria for establishing the many different groups of claims

are not understood from the Office Action. For example, claims to very similar methods for identifying mutations carried by the human SPG4 gene - claims 10, 11, 24, 25, 31 and 32 - are divided into three separate groups. That is, Groups VI and XII are directed to the same inventive concept. Moreover, there is a technical relationship between at least the claims of Groups I, II, IV, V, VI and XII. Applicants respectfully assert that at least these groups of claims are related as being products and a process for use of the products and should be examined together. In the alternative, at least Groups VI and XII should be examined together with new claims 41-71 submitted with this response.

In paragraph 4 of page 4, the Examiner imposes an "election of species" requirement, which is not required in unity of invention practice under Rule 13 of the PCT Rules. This election requirement is based on an interpretation of the "Instructions Concerning Unity of Invention" (Annex B, Unity of Invention, Part I, of Administrative Instructions Under the PCT) that allows the guidelines for consideration of Markush claims for chemical compounds to reach into method claims such as claims 31 and 32 by their dependency on claim 1, and determine the scope of the claims to be examined. Applicants submit that the application of the election of species requirement is not correct.

Section (f)(i)(B)(1) of Annex B states:

(i) When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

(A) all alternatives have a common property or activity, and

(B)(1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives, or

(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

According to the Examiner, "Section (f)(i)(B)(1) of Annex B of the Administrative Instructions requires that all alternatives of a Markush Group have a common structure which is a significant structural element."

Applicants submit that the alternatives of the sequences that are the subject matter of claim 1 meet the criteria of section (f)(i)(B)(2), thus fulfilling criteria (A), (B)(1) and (B)(2). As explained in section (f)(iii), "there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention." All the members of the class of isolated nucleic acids can be used in the same way and can be expected to behave in the same way (as probes, primers, nucleic acids in hybridization reactions, for example) in the methods of the claims, as is understood by those of ordinary skill in the relevant art. There can be no doubt, for example, that SEQ ID No. 1 and SEQ ID No. 2 are closely related, as genomic DNA and cDNA nucleotide sequences. The prober or primer of claim 24, which is a nucleic acid sequence of claim 5, are at least alternatives that belong to the class defined in claims 1 and 5. The requirement that there be a technical relationship among the members of the group of nucleic acids within claim 1 is met. Applicants assert that an election of species is therefore inappropriate and respectfully ask that the requirement be withdrawn.

The Administrative Instructions Under the PCT, Annex B, Unity of Invention, Part 1, "Instructions Concerning Unity of Invention," section (c)(iii) states, in part that,

"Where a search of the prior art is made, an initial determination of unity of invention, based on the assumption that the claims avoid the prior art, may be reconsidered on the basis of the results of the search of the prior art." Following a search of the prior art, no Invitation to Restrict or to Pay Additional Fees was issued in PCT/FR00/02433, indicating that the International Preliminary Examination Authority found unity of invention among the entire set of claims. Even though the Examiner has cited no new prior art that could change a determination of unity of invention, she has given Applicants a radically different interpretation of unity of invention of the claims – seventeen groups instead of one. The Examiner has not sufficiently explained her reasoning, in terms of unity of invention criteria, to justify such an extremely different interpretation.

Applicants respectfully request reconsideration and withdrawal of the restriction requirement and election of species requirement. Applicants further suggest that it would be proper for the claims of Groups VI and XII, claims 10-11 and 31-32, to be examined together as the inventions of at least these claims possess unity of invention. They further assert that claims 1-6, 24 and 25 should also be examined with Groups VI and XII.

Respectfully submitted,

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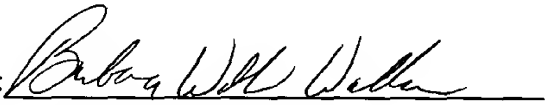
By: 
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